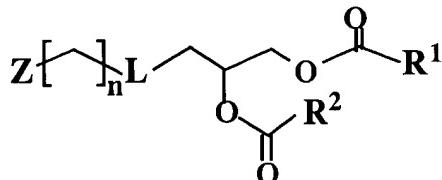


Amendments to the Specification:

On page 3, amend the paragraph beginning on line 1 as follows:

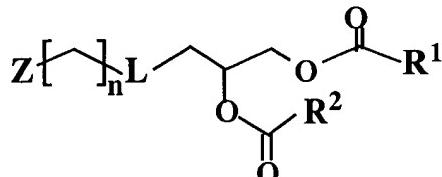
In one aspect, the invention includes a liposome composition containing a lipid represented by the formula:



*a<sup>1</sup>*  
wherein each of R<sup>1</sup> and R<sup>2</sup> is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms; n = 10-20; L is selected from the group consisting of (I) -X-(C=O)-Y-CH<sub>2</sub>-, (ii) -X-(C=O)-, and (iii) -X-CH<sub>2</sub>-, wherein X and Y are independently selected from oxygen, NH, and a direct bond; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

On page 6, amend the paragraph beginning on line 19 as follows:

In one aspect, the invention includes lipids represented by the structure shown below:



*a<sup>2</sup>*  
wherein each of R<sup>1</sup> and R<sup>2</sup> is an alkyl or alkenyl chain having between about 8 to about 24 carbon atoms; n = 10-20; and in a preferred embodiment is between 1-10; L is selected from the group consisting of (i) -X-(C=O)-Y-CH<sub>2</sub>-, (ii) -X-(C=O)-, and (iii) -X-CH<sub>2</sub>-, wherein X and Y are independently selected from oxygen, NH, and a direct bond; and Z is a weakly basic moiety that has a pK of less than about 7.4 and greater than about 4.0.

On page 7, amend the paragraph beginning on line 15 as follows:

*a<sup>3</sup>*  
The lipids of the invention include a neutral linkage, L, joining the Z moiety and the tail portion of the lipid. Linkage L can vary, but in one embodiment is selected from

*a3*  
coned

a carbamate, and ester, and amide, a carbonate, a urea, an amine, and an ether. In a preferred prepared lipid, a carbamate linkage is employed, wherein L is  $-X-(C=O)-Y-$   $CH_2-$ , X is NH, and Y is oxygen.

*a4*

On page 7, amend the paragraph beginning on line 24 as follows:

The lipid of the invention can be prepared using standard synthetic methods. A lipid was prepared having the structure shown above, wherein Z is an imidazole,  $Nn=2$ , L is a carbamate, and  $R^1 = R^2 = C_{17}H_{35}$ . A reaction scheme for preparation of this lipid is shown in Fig. 1. Full details of the synthesis are also provided in Example 1. Briefly, the para-nitrophenyl carbonate of 1,2-distearoyl glycerol (Compound I) and para-nitrophenyl chloroformate (Compound II) and reacted with histamine (Compound IV), to yield a lipid (compound VI) having an imidazole moiety linked to a distearoyl tail via a carbamate linkage. A similar synthesis, using glycerol in place of 1-amino-2,3-propanediol, can also be used to produce a carbonat-linked product (L =  $-O-(C=O)-O-$   $CH_2-$  or  $-O-(C=O)-CH_2-$ ).

*a5*

On page 8, amend the paragraphs beginning on line 4 and ending on 18 as follows:

Given the guidance and examples herein, other synthesis of a lipid having other linkages can be readily accomplished by those of skill in the art. Other linkage include, for example, ether (L = O-CH<sub>2</sub>-) and ester linkages (L = -O-(C=O)-), as well as urea amide, urea and amine linkages (i.e., where L = -NH-(C=O)-NH-, -NH-(C=O)-CH<sub>2</sub>-, -NH-(C=O)-NH-CH<sub>2</sub>-, or -NH-CH<sub>2</sub>-). A keto linkage, where L-X is a direct bond, may also be prepared. Figs. 2A-2B illustrate preparation of an etheramine-linked lipid (Fig. 2A) and an ester-linked-lipid having an NH-containing linkage (Fig. 2B), respectively. In Fig. 2A, the terminal amine of histamine is reacted with glycidyl chloride, hydrolyzing the resulting epoxide and acylation the resulting diol.

In Fig. 2B, an ester-linked-lipid having an NH-containing linkage (L = -O-(C=O)- or  $\underline{-O-(C=O)-CH_2-}$ ) is prepared, for example, by reacting histamine with an activated derivative of glyceric acid acetonide (2,2-dimethyl-1,3-dioxolane-4-carboxylic acid) or the four-carbon homolog, 2,2-dimethyl-1,3-dioxolane-4-acetic acid. The diol is subsequently deprotected and acylated.